

AMENDMENTS TO THE SPECIFICATION

Please insert the paper copy of the sequence listing submitted herewith into the specification at the appropriate space.

Please delete the paragraph at page 1, lines 19 – 27 of the originally-filed specification, and replace with the following paragraph:

Vertebrate telomeres consist of tandem repeats of the sequence TTAGGG (SEQ ID NO: 2) and associated proteins, which cap the ends of chromosomes and protect them from degradation and fusion (Blackburn E. H., *Cell* 106: 661-673, *Nature* 408(6808): 53-6, 2001). Extensive evidence has shown that telomere shortening and dysfunction in cultured somatic cells leads to so-called replicative senescence (Blackburn E.H., *Nature* 408(6808): 53-6, 2000). In turn, reversal of telomere shortening by forced expression of telomerase rescues cells from senescence and extends cell life span indefinitely (Bodnar, A. G., M. Ouellette, et al., *Science* 279(5349): 349-52, 1998). (Vaziri and Benchimol et al., *Curr Biol* 8(5): 279-82, 1998).

Please delete the paragraph spanning page 18, line 27 – page 19, line 5 of the originally-filed specification, and replace with the following paragraph:

The term “telomere” is intended to mean the modified end of an eukaryotic chromosome which contains repeated sequences of DNA. In humans, telomeres are composed of many kilobases of simple tandem 5'-TTAGGG (SEQ ID NO: 2) repeats (Moyzis *et al.* (1988) *Proc. Natl. Acad. Sci. U.S.A.* 85:6622). During DNA synthesis, the termini of the chromosomes are not fully replicated (Watson (1972) *Nature New Biology* 239:197,) by the action of DNA polymerase. Incomplete replication occurs at the 3' end of each of the two template strands of the chromosome, because the RNA primer needed to initiate synthesis in effect masks the 3' end of the template. The RNA primer is degraded after strand synthesis, and, as there are no additional sequences beyond the 3' end of the template to which primers can anneal, the portion

of the template to which the RNA primer hybridized is not replicated. In the absence of other enzymes, the chromosome is thus shortened with every cell division.

Please delete the paragraph at page 20, lines 6 -- 10 of the originally-filed specification, and replace with the following paragraph:

The term "telomere repeats" is intended to mean tandem repeats of a specific nucleotide sequence found within the telomeres at the end of chromosomes. In humans and other vertebrates, the telomere repeats are commonly tandem repeats of the sequence TTAGGG (SEQ ID NO: 2). The number of these tandem repeat sequences, present at the ends of a chromosome, determine the telomere length of a chromosome.

Please delete the paragraph at page 29, lines 26 -- 32 of the originally-filed specification, and replace with the following paragraph:

To determine the standardized average length of a telomere against which to compare telomere length in oocytes from women with reproductive problems, telomere length is determined from spare oocytes and polar bodies of control oocytes. Telomere lengths are determined by the number of tandem repeats of a specific nucleotide sequence found within the telomeres at the end of chromosomes. In humans and other vertebrates, the telomere repeats are commonly tandem repeats of the sequence TTAGGG (SEQ ID NO: 2).

Please delete the paragraph at page 32, lines 3 -- 26 of the originally-filed specification, and replace with the following paragraph:

Telomere length is determined by quantitative digital microscopy and integrated optical density of the fluorescence signal. The signal from the FITC-labeled probe hybridized to the telomeres is detected using a Zeiss fluorescence microscope (Axiophot) with a FITC filter.

Images of fluorescing telomeres are captured using an AxioCam digital microscope camera using AxioVision 2.0 software. Commercially available software, including MetaMorph (Universal Imaging CorporationTM, Downingtown PA), is used to integrate the fluorescent intensity and area. The digital images are then used for quantitative analysis of telomere length based on criteria described in Zijlmans *et al.* (1997). Background is subtracted and integrated fluorescence intensity in individual telomeres of chromosome spreads is measured to indicate the length of telomeres (Zijlmans *et al.*, 1997; Romanov, *et al.* Nature. 409:633-637 (2001)). The intensity of the fluorescence from each telomere is expressed in "Telomere Fluorescence Units" or "TFUs" and plotted on a graph for comparative purposes. Determined telomere lengths of the spare oocytes are compared to the results obtained for the control oocytes to establish whether the spare oocyte telomere lengths are abnormal. If the determined length of the oocyte's telomeres is found to be abnormal in comparison to the control or standardized average length, the batch of oocytes is considered at risk for aneuploidy and not fertilized for IVF purposes. If, however, the telomere length of the spare oocytes is found to be comparable to the control, the population of oocytes is not considered at risk for aneuploidy and is used for IVF procedures. Telomere lengths are determined by the number of tandem repeats of a specific nucleotide sequence found within the telomeres at the end of chromosomes. In humans and other vertebrates, the telomere repeats are commonly tandem repeats of the sequence TTAGGG (SEQ ID NO: 2).

Please delete the title at page 34, line 11 of the originally-filed specification, and replace with the following title:

Detection of TTAGGG (SEQ ID NO: 2) repeats at chromosome telomeric ends

Please delete the paragraph at page 34, lines 13 – 19 of the originally-filed specification, and replace with the following paragraph:

To detect the presence of TTAGGG (SEQ ID NO: 2) repeats at the chromosome ends, the number of repeats comprising the telomeric ends determine the length of the telomeres,

telomeric FISH was performed on oocyte metaphase spreads using a fluorescent FITC-labeled (CCCTAA)₃ (SEQ ID NO: 10) peptide nucleic acid (PNA) probe, which is able to detect 200 bp of TTAGGG (SEQ ID NO: 2) repeats at the telomeres. FISH was employed to measure telomere length in chromosomes spread from spare eggs matured from the GV stage after aspiration from consenting subjects undergoing ART and ICSI (Figure 1).